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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,795	07/09/2003	Andrew J. Dannenberg	CRF D-2756 NB	8535

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EXAMINER	
ROBERTS, LEZAH	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
01/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/614,795	DANNENBERG ET AL.	
	Examiner	Art Unit	
	LEZAH W. ROBERTS	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6-11* is/are pending in the application.

4a) Of the above claim(s) *7, 8, 9 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the Amendment filed July 18, 2008. All rejections have been withdrawn unless stated below.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims

Claim Rejections - 35 USC § 103 – Obviousness

1) Claims 6 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seibert et al. (US 5,972,986) in view of Jaradat et al. (Biochemical Pharmacology 2001) and Mestre et al. (Annals of the New York Academy of Sciences 1999). The rejection is maintained.

Applicant's Arguments

Applicant argues the claimed invention is directed to a method for screening selective inhibitors of COX-2 for therapeutic functionality (i.e., off-target effects) in addition to COX-2 protein inhibition (i.e., target effect). None of the above-identified publications, alone or in combination, suggest screening for the off-target effects of selective COX-2 inhibitors, or using a plurality of tests as recited in claim 6. SEIBERT neither discloses nor suggests screening for the off-target effects of selective COX-2 inhibitors. Moreover, there is no recognition that some COX-2 inhibitors may be more effective than others in light of their off-target effects. Applicants respectfully submit that

JARADAT fails to remedy the deficiencies of SEIBERT. SEIBERT leads one skilled in the art to use selective inhibitors of COX-2 and JARADAT focuses on the effects of NSAIDs, it is believed that one skilled in the art would lack the motivation to combine and modify the teachings of Seibert and JARADAT. The chemical structure and function of selective COX-2 inhibitors are distinct from the chemical structure and function of NSAIDs. Moreover, while JARADAT states that the effect of NSAIDs may be related to both inhibition of PGHS enzymes and to activation of PPAR, the word may does not provide one skilled in the art a reasonable expectation of success to combine and modify the publications in a manner that would result in a meaningful outcome. MESTRE studies the inhibition of COX-2 as an approach to preventing head and neck cancers. In particular, MESTRE test for the suppression of EGFR mediated production of COX-2 with retinoids. However, MESTRE does not teach that selective COX-2 inhibitors exhibit this function. Moreover, such suppression is different from a decrease in the levels of or down regulation of expression of the compounds recited in the class 1 family of receptors of tyrosine kinase of claim 6 (e.g., see step (b)). In imposing the rejection, the Official Action appears to believe that because overexpression of COX-2 has been associated with different cancers, it would have been obvious to look for different ways to determine COX-2 inhibition as discussed in the JARADAT and MESTRE publications. However, applicants respectfully submit that this position does not take into consideration that the claimed invention is directed to a method for screening selective inhibitors of COX-2 for therapeutic functionality (i.e., off-target effects) in addition to COX-2 protein inhibition. Indeed, as noted above, none of the

publications suggest specifically screening for the off- target effects of selective COX-2 inhibitors, or using a plurality of tests as recited in claim 6.

Examiner's Response

Although Sierbert does not disclose screening methods, it does disclose COX-2 inhibitors are used for the treatment of neoplasia (see Abstract). It also discloses COX-2 has been observed in neoplastic disease and inhibitors of COX-2 are used to treat neoplasia that produces prostaglandins. The reference also discloses that COX-2 inhibitors were more effective than a non selective COX-1/COX-2 inhibitor (Table 1) and using a COX-2 inhibitor instead of NSAIDs is more effective for treating inflammation and produces fewer sided effects (col. 1, lines 27-35). The reference provides the motivation of why one would want to screen COX-2 selective inhibitors to treat cancer. The secondary reference, Jaradat et al., discloses inhibition of prostaglandins is the molecular basis for inflammatory action for NSAIDS. The reference also discloses future testing using PGHS-2 inhibitors as regulators of PPAR isoforms, which encompass COX-2 selective inhibitors. Therefore the secondary reference suggests using PGHS-2 inhibitors for activating PPAR isoforms. Further Jaradat et al. discloses PPAR activation inhibits the induction of PGHS-2. PPAR also has a role in the regulation of inflammatory processes in the body. Therefore it would have been obvious to test COX-2 inhibitors of the primary reference by screening for PPAR activation to help determine if the inhibitor would be successful in treating the neoplasia in the primary reference by inhibiting the production of prostaglandins by inhibiting the induction of PGHS-2 or COX-2. In regards

to applicant's assertion that NSAID may be related to both inhibition of PGHS enzymes and to activation of PPAR, Applicant has not pointed out where this statement is found. In any case, the reference also states, NSAIDs activate and bind to PPAR isoforms (page 1588, second paragraph). Further, the claims use the term likelihood, based on Applicant's reasoning, the term likelihood does not provide one skilled in the art a reasonable expectation of success that the inhibitors will treat cancer based on the screening methods of the claims. Mestre teaches compounds that downregulate EGFR and inhibit EGF-mediated induction of COX-2. Therefore it would have been obvious to screen COX-2 inhibitors for the ability to downregulate EGFR. This down regulation would in turn down regulate COX-2 which would lead to lower formation of prostaglandins. Applicant's assertion "the suppression of EGFR mediated production of COX-2 is different from a decrease in the levels of or downregulation of expression of the compounds recited in the class 1 family of receptors of tyrosine kinase of claim 6 (e.g., see step (b)) is not explained. One of skill in the art would reasonably conclude that the inhibition of EGF-mediated induction of COX-2 occurs from the downregulation of EGFR and downregulation of EGFR would lead to downregulation of COX-2 which leads to a decrease in prostaglandins. Therefore one of skill in the art would also reasonably conclude that if the COX-2 inhibitors of the primary reference could downregulate EGFR than it would be likely that these compounds are likely to treat cancer. It would be reasonably expected that the more mechanisms of producing prostaglandins a compound can hinder, the more likely that compound will inhibit formation of prostaglandins in cancer. Therefore it would be obvious to screen a

compound for its ability to inhibit COX-2 by different paths. The more paths that are inhibited the more likely the compound will inhibit prostaglandin production and the more likely it will be more effective in treating cancer. Further claims do not recite that a-g are off target effects. Even if this was the case, the reason or motivation to modify a reference may often suggest what the inventor has done but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See MPEP 2144, IV. The screening techniques are all related to COX-2 and therefore it is reasonable to conclude that one of skill in the art would use the techniques to determine their effectiveness as COX-2 inhibitors as well as determining their likelihood to decrease prostaglandin production for the treatment of conditions like cancer. The higher the likelihood of inhibiting prostaglandin production, the higher the likelihood the compound will be effective in treating cancer.

Claims 6 and 10 are rejected.

Claims 7-9 and 11 are withdrawn.

No claims allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LEZAH W. ROBERTS whose telephone number is (571)272-1071. The examiner can normally be reached on 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lezah W Roberts/

Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612